WEST VIRGINIA Department of Health & Human Resources

COVID-19

CLINICAL GUIDANCE FOR HEALTHCARE PROFESSIONALS

This guidance is based on currently available information and resources and is subject to change

This guidance was created by healthcare professionals, including infectious disease, pulmonary, and intensive care physicians, and pharmacists, working in the state of West Virginia to use as reference to better guide treatment of patients with suspected or confirmed COVID-19. It is intended as a guide and does not contain every possible COVID-19 presentation. It should not replace clinical judgement or other available clinical guidance as appropriate. Clinicians are strongly encouraged to remain up to date with evolving recommendations and to adapt their practices as more evidenced-based management and treatment guidance emerges.

Novel Coronavirus Background

On December 31, 2019, a pneumonia of unknown cause from Wuhan, China, was reported to the China World Health Organization (WHO) Country Office. This illness was later determined to be caused by a coronavirus called SARS-CoV2. In mid-February 2020, the WHO announced a name for the new disease: COVID-19. On March 11, 2020, the WHO declared the COVID-19 viral disease a pandemic.

Geographic Distribution and Transmission

The outbreak is thought to have started in a live animal and seafood market in Wuhan, China. The number of cases in China spread quickly, and there is now evidence that spread has slowed in China due to mandatory stay-at-home orders. The first case in the United States was reported January 22, 2020, in Washington State. Community spread in the United States is now occurring and there are currently more cases of COVID-19 reported in the United States than in any other country.

Person-to-person transmission of COVID-19 occurs mainly when respiratory droplets (when a person coughs, sneezes, etc.) from an infected person come into direct contact with the mucous membranes of an uninfected person. Asymptomatic and presymptomatic infections are thought to occur, but their frequency and role in transmission are not completely understood. The virus can survive on surfaces for several days and transmission can occur if a person touches an infected surface and then touches their eyes, mouth, or nose. This is why hand washing for 20 seconds with soap and water or use of an alcohol-based sanitizer (at least 60% alcohol) and thorough environmental cleaning is so important, and also why it is critical to avoid touching your face.

Maintaining 6-feet social distancing remains critical in slowing the spread of the COVID-19. As of April 3, 2020, the Centers for Disease Control and Prevention (CDC) is advising the use of simple cloth face coverings to slow the spread of the virus and prevent transmission by those who may unknowingly have the virus. Cloth face coverings fashioned from household items or made at home from common materials can be worn in public settings where other social distancing measures may be difficult to maintain. Non-healthcare workers should wear these alternative forms personal protective equipment (PPE) as part of their protection AND should continue to emphasize and rely heavily on social (physical) distancing.

Incubation Period

The incubation period for COVID-19 is thought to be within 14 days, but most cases occur within 4-6 days after exposure.

Clinical Presentation

Clinical Signs/Symptoms	Prevalence
Fever	44-98%
Cough	46-82%
Shortness of Breath	20-64%
Myalgia/Fatigue	50-88%
Sore Throat/Rhinorrhea	15-50%
GI Symptoms (loss of sense of smell/taste, nausea, vomiting, diarrhea)	10-50%

Most patients (~80%) with COVID-19 have mild symptoms. Patients with mild disease can often be monitored at home and kept in isolation to prevent spread of infection to others.

Patients with moderate to severe disease have dyspnea and hypoxia. They typically require hospital admission and oxygen therapy. Patients with severe/critical disease have respiratory failure, shock, and multiorgan dysfunction. They typically require admission to the intensive care unit and require mechanical ventilation.

RISK FACTORS FOR SEVERE DISEASE
Age greater than 60 years old
Asthma or chronic lung disease
Diabetes
Heart disease
Hypertension
Immunosuppressing conditions or medications
Living in a long-term care facility or nursing home
Obesity (BMI > 40)
Pregnancy

Most patients will have a normal white blood cell count. Many will have elevated inflammatory markers including CRP, D-dimer, and ferritin. Lymphopenia, elevated liver enzymes, elevated LDH, elevated inflammatory markers, elevated troponin, elevated creatinine kinase, and acute kidney injury are associated with worse outcomes. Chest x-ray and CT scans will often show bilateral ground glass opacifications.

Testing

Currently, diagnosis of COVID-19 is made by SARS-CoV2 PCR testing. CDC recommends collection of a nasopharyngeal swab specimen. If the patient is intubated, the PCR may be performed on a bronchoalvelolar lavage or sputum specimen and actually has a higher sensitivity than the nasopharyngeal specimen. The nasopharyngeal PCR test can be negative very early in disease development when the viral load is not high enough to be detected. Thus, in those patients with high suspicion for having COVID-19 (i.e., close contact with a confirmed case and symptoms consistent with disease) an initial negative test may not rule out disease. Serologic tests are not generally available at this time.

In general, it is not recommended to test asymptomatic patients, unless there is rare exception made to test for cases that have public health implications, such as outbreaks or other identified need for surveillance. Although it may be ideal to know for diagnostic purposes, it is not necessary to test all individuals with mild disease as they should be managed presumptively.

The Infectious Disease Society of America (IDSA) has provided guidance on which patients to test for COVID-19. **Testing should be prioritized based on availability of testing in your area.**

Tier 1 Patients:

- Critically ill patients with unexplained symptoms.
- Individuals with respiratory symptoms and contact with positive COVID-19 patient or recent travel to areas with high community transmission.
- Patients with fever or respiratory infections who are also immunocompromised (including those with HIV), elderly, or have underlying chronic conditions.
- Individuals critical to pandemic response who experience respiratory symptoms (health care workers, public health officials, and other essential leaders).

Tier 2 Patients:

- Non-ICU hospital patients and long-term care residents with symptoms.

Tier 3 Patients:

- Patients in outpatient settings who meet the criteria for influenza testing including those with select co-morbid conditions such as diabetes, COPD, congestive heart failure, pregnant women, and symptomatic children with additional risk factors.

Tier 4 Patients:

- Individuals in communities being monitored by health authorities to collect data and ascertain prevalence of COVID-19.

It is crucial to remind patients and their family members/close contacts to isolate/self-quarantine while waiting for test results to return. Patients admitted to the hospital are automatically placed in enhanced droplet isolation (or airborne if aerosolizing procedure being performed) but for those tested as outpatients, appropriate guidance should be provided.

Management

The management for COVID-19 is supportive care, only including symptomatic treatment and supplemental oxygen when needed. It is generally recommended to avoid NSAIDs and steroids in these patients. There are no approved antiviral medications for the treatment of COVID-19. There is not currently an approved vaccine for prevention. Some medications are being used off-label in investigational use for select patients with moderate or severe/critical disease. This includes hydroxychloroquine, remdesivir, and/or tocilizumab. However, there is no clear evidence of the efficacy of these drugs at this time. This will change as more clinical trials are conducted. **These medications should not be used in mild disease patients as the risk may outweigh the benefit.** In moderate to severe disease patients, these may be used on a case by case basis based on clinical judgement and expertise including considering consultation with ID and ICU specialists. Chloroquine phosphate, when used without a prescription and supervision of a healthcare provider, can cause serious health consequences, including death. It is advised that chloroquine, and the related compound hydroxychloroquine, should only be used under the supervision of a healthcare provider as prescribed medications.

Treatment Considerations:

- Recommend symptom and risk level assessment to help determine clinical management
- If suspicion of COVID-19 AND alarming symptoms, treat empirically as confirmed case in appropriate disease category until test result is received

- Drug recommendations are currently not FDA-approved for the treatment of COVID-19 and decisions for use should follow a risk-benefit discussion with individual patients and treatment teams
- Recommendations are subject to change based on emerging data and drug availability

For all patients with suspected or confirmed COVID-19:

- Limit staff exposure time as much as possible
- Minimize ancillary testing (e.g., blood draws) and services as able
- Avoid procedures unless absolutely indicated such as ECHO
- Metered-Dose Inhaler (MDI) should be used when able, avoid nebulizers
- Monitor for signs and symptoms of cardiomyopathy

Mild Disease – symptoms WITHOUT oxygen requirement, no evidence of pneumonia

Recommend supportive care:

- Conservative fluid management
- Symptomatic treatment
- Manage comorbid conditions, especially those considered high risk
- Avoid corticosteroids unless otherwise indicated
- Avoid NSAIDs

Moderate Disease – symptoms WITH oxygen requirement, evidence of pneumonia

- Provide oxygen therapy as needed
    - If worsening respiratory status, mechanical ventilation is favored over noninvasive ventilation methods
- Supportive care
- Consider hydroxychloroquine (off-label) if no contraindications in high-risk patients
    - 400mg PO BID day 1
    - 200mg PO BID day 2-5
    - *Caution use of hydroxychloroquine in QTc prolongation, epilepsy, myasthenia gravis, drug interactions and monitor closely for QTc prolongation especially in combination with other QTc prolonging medications, such as azithromycin
- Consider antibiotics or antifungals for bacterial and opportunistic infections when appropriate
    - Follow current treatment recommendations for community-acquired pneumonia (CAP) or hospital-acquired (or nosocomial) pneumonia (HAP)/ventilator-associated pneumonia (VAP)
    - Azithromycin is drug of choice for atypical CAP coverage in COVID+ patients
        - 500mg PO once day 1
        - 250mg PO daily day 2-5
    - If facility starts empiric coverage for MRSA, de-escalate as able and indicate using MRSA nasal swab and culture data where available

Severe/Critical Disease – symptoms, evidence of pneumonia, ARDS, multi-organ failure, and/or sepsis requiring mechanical ventilation

- Intensive Care status
- Mechanical ventilation (low tidal volume ventilation 4-8L)
- Avoid fluids being cognizant of hidden fluids in IV antibiotics and other medications and infusions
- Manage comorbid conditions, especially those considered high-risk
- Avoid corticosteroids unless otherwise indicated
- Avoid NSAIDs

- Albuterol may be considered for respiratory distress. Use of Metered-Dose Inhaler (MDI) over nebulization is recommended where able
- Consider hydroxychloroquine (off label) if no contraindications in high-risk patients
    - 400mg PO BID day 1
    - 200mg PO BID day 2-5
    - *Caution use of hydroxychloroquine in QTc prolongation, epilepsy, myasthenia gravis, drug interactions and monitor closely for QTc prolongation especially in combination with other QTc prolonging medications, such as azithromycin
- Consider antibiotics or antifungals for bacterial and opportunistic infections when appropriate
    - Follow current treatment recommendations for CAP or HAP/VAP
    - Azithromycin is drug of choice for atypical CAP coverage in COVID+ patients
        - 500mg PO once day 1
        - 250mg PO daily day 2-5
    - If facility starts empiric coverage for MRSA, de-escalate as able and indicate using MRSA nasal swab and culture data where available
- Consider contacting Gilead drug manufacturer for information on use of investigational drug, remdesivir. Information on use and availability of this medication for COVID-19 treatment is rapidly changing
- Consider tocilizumab (off-label) if patient progresses to meet criteria for cytokine storm
    - Dose: 400mg IV x 1 dose
    - Must be cognizant of ALT elevations
        - Hyperinflammatory states and cytokine release syndrome, including elevated IL-6, has been reported in severe COVID-19 and associated with increased mortality in patients
        - Consider trending hyper-inflammatory syndrome labs
            - CRP, fibrinogen, ferritin, d-dimer, LDH
- Treat ARDS and Sepsis according to current recommendations and protocols

Signs and symptoms of cytokine release syndrome

Organ System	Symptoms
Constitutional	Fever ± rigors, malaise, fatigue, anorexia, myalgias, arthralgias, nausea, vomiting, headache
Skin	Rash
Gastrointestinal	Nausea, vomiting, diarrhea
Respiratory	Tachypnea, hypoxemia
Cardiovascular	Tachycardia, widened pulse pressure, hypotension, increased cardiac output (early), potentially diminished cardiac output (late)
Coagulation	Elevated D-dimer, hypofibrinogenemia ± bleeding
Renal	Azotemia
Hepatic	Transaminitis, hyperbilirubinemia
Neurologic	Headache, mental status changes, confusion, delirium, word finding difficulty or frank aphasia, hallucinations, tremor, altered gait, seizures

Modified grading scale of cytokine release syndrome for COVID-19 patients

Grade	Toxicity	Treatment Consideration
1	Symptoms are not life threatening and require symptomatic treatment only	Supportive care
2	Symptoms require and respond to moderate intervention FiO_2 ≤40% on mechanical ventilation or Hypotension responsive to fluids or low dose vasopressors	Supportive care
3	Symptoms require and respond to aggressive intervention FiO_2 >40% on mechanical ventilation or Hypotension requiring high dose or multiple vasopressors or Worsening clinical status	Supportive care **Consider tocilizumab**
4	Life threatening symptoms or Multi-organ dysfunction	Supportive care **Consider tocilizumab**

Other considerations

Therapies to AVOID:

- **NSAIDs**: No evidence to support use of mitigating inflammatory response in COVID-19 and potential to exacerbate kidney injury in severe illness
- **Corticosteroids**: May prolong viral shedding. Could be used if other compelling indications
- **Ribavirin:** Insufficient evidence to support use in SARS and some evidence for poorer outcomes. Carries toxicities which can lead to discontinuation such as reduced hemoglobin concentrations
- **Interferon:** Insufficient evidence to support use and risk of toxicity
- **Lopinavir:** Randomized controlled trial observed no benefit in adults hospitalized with severe COVID-19
- **Darunavir:** Statement from Johnson & Johnson: no clinical evidence to support use for COVID-19
- **IVIG:** Insufficient evidence to support use for COVID-19
- **Bronchoscopy:** Aerosol generating procedure which poses risk to patients and staff

Methods:

This guidance was developed based upon review and compilation of currently available clinical guidance and protocols created by clinical experts at teaching hospitals in West Virginia. This guidance was reviewed and edited by content experts across the state, including all academic institutions and multiple community-based practitioners.

References:

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